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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,430	03/09/2005	Jeffery A Bibbs	DIAKR.007NP	5428

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EXAMINER

BETTON, TIMOTHY E

ART UNIT	PAPER NUMBER
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1617

NOTIFICATION DATE	DELIVERY MODE
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10/06/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/527,430	Applicant(s) BIBBS, JEFFERY A	
	Examiner TIMOTHY E. BETTON	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4,5 and 7-11 is/are pending in the application.
- 4a) Of the above claim(s) 7-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4, and 5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' Response filed on 14 May 2009 has been acknowledged and duly made of record.

In view of the amendment to claim 1 to recite limitations explicitly to those antagonists encompassed by formula I, the rejection under 35 USC SECTION 112, 1st paragraph is hereby withdrawn.

Applicants' further argue in the 102(b) rejection that the limitation drawn to "in regular doses no more often than once per day" is not anticipated by Kumar et al.

Applicants' arguments are considered but are not found persuasive because the limitation "in regular doses no more often than once per day" is an inherent use of any pharmaceutical composition administered by mouth to a patient in need of such treatment. It would be instantly apparent to the one of skill in the pertinent art that a T-channel agonist oral composition would be given *at least* once per day which reasonably encompasses in anticipation the limitation of the current invention which discloses "in regular doses no more often than once per day".

Applicants' render no response to the 103(a) rejection of the said previous office action filed on 21 January 2009.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1, 2, 4, and 5 are pending further prosecution on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Kumar et al. Kumar et al. teach the elected species as described above (please see page 651, structure of first column, represented by PPK 1-16, specifically see Table 1, PPK-5, which teach each and every constituent as elected for formula 1, wherein R is CH (CH₃)₂, R₁ is CH₃, R₂ is CH₃, R₉ of the current invention is identically duplicated on structure PPK 1-16.

Kumar et al. teach the use of PPK-5 (the moiety that teaches on the elected compound specifically) in the blocking of T-Type Calcium Channels (see page 654, column 1, 1st full paragraph).

Thus, Kumar et al. teach the current invention in view of the limitations disclosed. The inherent activities of T-Type Calcium Channel Antagonists are also adequately supported and suggested by Kumar et al. based on Figure 6, parts A and B, which teach and elucidate the

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anticipated activity of PPK-5 in comparison to Nifedipine, a well-known T-Type Calcium Channel Antagonist.

With regard to the limitation “in regular doses no more often than once per day”, the MPEP cites thus:

I. SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE

UPON THE DISCOVERY OF A NEW PROPERTY

“[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). **Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.** *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), [...].**The court stated that “just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.”**

Id.< See also MPEP § 2112.01 with regard to inherency and product-by-process claims and MPEP § 2141.02 with regard to inherency and rejections under 35 U.S.C. 103.

Thus, the limitation “in regular doses no more often than once per day” is an inherent use of any pharmaceutical composition administered by mouth to a patient in need of such treatment. It would be instantly apparent to the one of skill in the pertinent art that a T-channel agonist oral composition would be given *at least* once per day which reasonably encompasses in anticipation the limitation of the current invention which discloses “in regular doses no more often than once

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per day”.

Further, absent of any indication in the specification with regard to what is meant by the term “regular”, the said term is given its broadest interpretation in view of the scope of the claimed invention. In this said case, a regular dose would be characterized as a concentration sufficient to affect a physiological change in a mammal body. Kumar et al. as a result fully anticipates the claimed invention by teaching a concentration ranging from 0.3 μM -3 μM of PPK-5 on transiently expressed on T-type channels obtained from 11 different cells (please see Figure 6, graphs A and B).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al. (Synthesis and Evaluation of a New Class of Nifedipine Analogs with T-Type Calcium Channel Blocking Activity, Mol. Pharmacol. 61: 649-658, 2002 in view of Kobrin et al. (Safety of Mibefradil, a New Once-A-Day, Selective T-Type Calcium Channel Antagonist, The American Journal of Cardiology, Vol. 80 [48], 1997, printed pages 1-7) in view of Li et al. (USPGPUB 2001/0049447 A1).

For the reasons already disclosed above, Kumar et al. is reapplied in obviousness over claimed invention.

Additionally, Kumar et al. teach the similarities with regard to mechanisms of action with the compound as elected and the drug, Nifedipine (page 654, col. 2, page 655, 1st col., 1st paragraph).

Kumar et al. does not teach “prodrug”.

However, Li et al. resolves the deficiency of Kumar et al. in view of the limitations contained in the current invention by teaching [...] prodrugs, the compounds of the present

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invention may additionally or alternatively be prepared to be delivered in a prodrug form. The term prodrug indicates a therapeutic agent that is prepared in an inactive form that is converted to an active form (i.e., drug) within the body or cells thereof by the action of endogenous enzymes or other chemicals and/or conditions [0021].

Li et al. teach embodiments replete with T-type channel antagonist such as nifedipine which was indicated in Kumar et al. as having similar P450 inhibition profile and mechanisms of action as the elected compound.

Li et al. does not teach once a day dosing of a T-Type channel antagonist.

However, Kobrin et al. resolves the deficiency in Li et al. by teaching the once a day dosing of Mibefradil, a conventional T- Type channel antagonists. Further, Kobrin et al. disclose methods which include nifedipine which was indicated in Kumar et al. as having the same affinity toward the same receptors as the chemical moiety as elected (PPK-5 in the Kumar reference) (please see Methods, 2nd column, 1st full paragraph).

Thus, it would have been prima facie obvious to the one of skill at the time of invention to recognize a reasonable expectation of success via the combining the incorporating together the teachings and methods of Kumar et al., Li et al. and Kobrin et al.

In determining the scope and content of the prior art, Kumar et al. adequately teach subject matter which is obvious over the claimed invention. Kumar et al. teach the elected moiety disclosed as PPK-5, which is similar in activity to nifedipine (a well-known selective inhibitor). Li et al. teach T-Type channel antagonists as prodrugs which makes claim 4 obvious. Kobrin et al. teach a pharmaceutical composition comprising an art-known T-type inhibitors

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such as Mibefradil and nifedipine which are indicated in a regimen for once-a-day administration.

In view of the teachings of Kumar et al., the said reference clearly teaches the similarities of nifedipine with regard to the elected species. The elected compound is taught expressly throughout the Kumar et al. reference. However, agents such as nifedipine are further elucidated with reference to clear therapeutic regimens. This is the ascertained difference between the prior art and the claims at issue.

In considering objective evidence present in the application indicating obviousness, the one of skill would readily be inclined to recognize that if nifedipine and Mibefradil exemplify the same mechanisms of action as the elected compound and/ or vice-versa, then the claimed invention is thus overcome by obviousness in the teachings and methods of the references disclosed *supra*.

With regard to the limitation “in regular doses no more often than once per day”, the MPEP cites thus:

I. SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE

UPON THE DIS-COVERY OF A NEW PROPERTY

“[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). **Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.** In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In

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In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), [...]. **The court stated that “just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.”**

Id.< See also MPEP § 2112.01 with regard to inherency and product-by-process claims and MPEP § 2141.02 with regard to inherency and rejections under 35 U.S.C. 103.

Thus, the limitation “in regular doses no more often than once per day” is an inherent use of any pharmaceutical composition administered by mouth to a patient in need of such treatment. It would be instantly apparent to the one of skill in the pertinent art that a T-channel agonist oral composition would be given *at least* once per day which reasonably encompasses in obviousness over the limitation of the current invention which discloses “in regular doses no more often than once per day”.

Further, absent of any indication in the specification with regard to what is meant by the term “regular”, the said term is given its broadest interpretation in view of the scope of the claimed invention. In this said case, a regular dose would be characterized as a concentration sufficient to affect a physiological change in a mammal body. Kumar et al. as a result fully anticipates the claimed invention by teaching a concentration ranging from 0.3 μM -3 μM of PPK-5 on transiently expressed on T-type channels obtained from 11 different cells (please see Figure 6, graphs A and B).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access

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to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617